REMARKS

Claims 21-29 were pending in the instant application. By this amendment, claims 7-20 have been canceled without prejudice to Applicants' right to pursue the subject matter of the canceled claims in this application or other related applications. Claims 23, 25, 27 and 29 have been amended, and new Claims 30-39 have been added to clarify the invention. No new matter is added.

1. OBJECTION TO THE SPECIFICATION

The specification is objected to as not complying with 37 C.F.R. 1.821(d) of the Sequence Rules and Regulations. In response, Applicants have amended the specification to add new SEQ ID NO: to the sequence listing and to add recitation of the new sequence identifiers to the specification where appropriate. New new matter is added.

A substitute Sequence listing in paper form and in computer readable (compact disc) form are submitted concurrently herewith. In accordance to 37 C.F.R. 1.821(f), Applicants submit that the sequence listing information recorded in computer readable form is identical to the paper form of the Sequence Listing.

2. OBJECTION TO THE CLAIMS

Claims 23-24 are objected to by the Examiner for their dependence upon canceled claims. Applicants submit that claim 23 contained a typographical error and have amended claim 23, thus, rendering the objection to claims 23 and 24 moot.

Claims 25-27 are objected to for improper multiple dependency. In response, Applicants have amended claim 25 to be dependent on any one of claims 21 or 22. Claim 27 has been amended to depend from claims 21 or 22. Claim 29 has been amended to depend on claim 4. New claims have been added to cover the subject matter canceled as a result of the amendment of claims 25-27. No new matter is added.

In view of the amendments made herein, it is submitted that the objections are avoided and moot.

3. THE REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, FOR LACK OF WRITTEN DESCRIPTION SHOULD BE WITHDRAWN

Claims 23 and 24 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Examiner contends that the specification does not provide written description support for substituting functions of hgro-1 polynucleotide for functions of *C. elegans* gro-1 since it was not demonstrated that fragments of hgro-1 gene can substitute for the *C. elegans* gene in the rescue of the e2400 mutant phenotype. The Examiner alleges that the specification did not contemplate a subregion of gro-1 or hgro-1 that would rescue the e2400 phenotype.

The criteria for determining sufficiency of written description set forth in Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112 ¶ 1, "Written Description" Requirement" ("the Guidelines") (published in the January 5, 2001 Federal Register at Volume 66, Number 4, pages 1099-1111), specifies that:

> "Whether the specification shows that applicant was in possession of the claimed invention is not a single, simple determination, but rather is a factual determination reached by considering a number of factors. Factors to be considered in determining whether there is sufficient evidenced of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function and the method of making the claimed invention." *Id.* at page 1106, column 2, lines 25-41.

Where the specification discloses any relevant identifying characteristics, *i.e.*, physical, chemical and/or functional characteristics, sufficient to allow a skilled artisan to recognize the applicant was in possession of the claimed invention, a rejection for lack of written description under Section 112, first paragraph, is misplaced.

Furthermore, in accord with the Written Description Guidelines, what is conventional or well known to one of skill in the art need not be disclosed in detail and where the level of knowledge and skill in the art is high a written description questions should not be raised (Fed. Reg. Vol. 66, no. 4, January 5, 2001, p. 1106).

Applicants submit that the specification disclosed a *C. elegans* gene consisting of 9 exons spanning 2 kb which was identified by use of a functional complementation assay based on *C. elegans* gro-1 (e2400) mutants. Although the cosmid clones identified by Applicants apparently contained the gro-1 gene, one of skill in the art would recognize that Applicants contemplated (i) cosmid clones and subclones that contain only a fragment of the gro-1 gene, and (ii) using a functional assay that can identify gro-1 fragments which retain functions of the gene. The skilled person and Applicants would have understood that the cosmid clones contained random fragments of the *C. elegans* genome, and that one end of a cosmid or its subclones may lie within the gro-1 gene.

Moreover, the specification disclosed that the human gro-1 gene was obtained by assembling fragments of hgro-1 nucleotide sequences that were identified by Applicants based on their sequence homology to the *C. elegans* gro-1 sequence (see specification at page 14, lines 1-28). Thus, fragments of human gro-1 gene and their homology with gro-1 sequences of other species, such as yeast and *E. coli* were disclosed in the specification as filed. Given the description of use of a functional assay to test gro-1 activity, and the sequence homology and the presence of the zinc finger motif in both human and *C. elegans* gro-1 (see Figure 9, page 14, lines 23-28), one of skill in the art would have understood Applicants to be in possession of the claimed invention at the time of filing. As pointed out in the previous Amendment, the level of skill in the art at the time of filing included *C. elegans* rescue assays where cDNAs from non-*C. elegans* species were introduced into mutant nematodes to rescue mutant phenotypes (see References BL and BM).

Applicants respectfully submit that disclosure of uncharacterized human

expressed sequence tags coupled with Applicants' teachings of their homology to the *C. elegans* gro-1 provided in the specification and the high level of skill in the art, clearly indicate that Applicants were in possession of the claimed invention.

In light of the foregoing reasoning, the rejection under 35 U.S.C. § 112, first paragraph for lack of written description support should be withdrawn.

4. THE REJECTION UNDER 35 U.S.C. § 101 FOR LACK OF UTILITY SHOULD BE WITHDRAWN

Claims 21-24 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well-established utility. The Examiner alleges that the reference of Golovko et al. fails to reach a utility for the disclosed isopentenyl transferase, and therefore, the instant isopentenyl transferase cannot rely on being a member in the class of human isopentenyl transferase for utility. The Examiner also asserts that the relation of the instant isopentenyl transferase to spontaneous mutagenesis, genome stability and cancer or epigenetic control of gene expression is not a credible utility without a specific enablement set forth in the specification. Applicants respectfully disagree.

According to applicable case law, "The threshold of utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit *Juicy Whip, Inc. v. Orange Bang, Inc.* 185 F.3d 1364, 51 U.S.P.Q.2d 1700 (Fed. Cir. 1999).

The claimed invention encompasses polynucleotides that encode a human isopentenylpyrophosphate:tRNA transferase ("IPT") or a fragment thereof that exhibits the functional activity of the enzyme, and vectors and host cells comprising said polynucleotides. One of the utilities of the claimed invention is the making of the highly-conserved functional human IPT for use as a test reagent in scientific and/or medical research.

According to MPEP 2107.01, a "specific utility" is *specific* to the subject matter claimed which contrasts with a *general* utility that would be applicable to the broad class of the invention. Here, the broad class of the invention include *any* polynucleotides and recombinant cells. In contrast, the claimed invention has the specific utility of producing an enzyme that catalyzes the transfer of an isopentenyl moiety from dimethylallyl pyrophosphate (DMAPP) to the adenosine immediately adjacent 3' to the anticodon of tRNAs whose anticodons terminate with uridine, resulting in N^6-(Δ^2-isopentenyl)adenosine ("i^6A"). Applicants point out that the broad class of the invention does not possess this specific utility. Hence, the claimed invention met the requirement of having a specific utility.

MPEP 2107.01 states that a "substantial utility" defines a "real world" use, and that utilities which require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. As examples, MPEP 2107.01 indicated that an assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would also define a "real world" context of use in identifying potential candidates for preventive measures or further monitoring.

In the present application, the specification teaches that a mutant gro-1 protein led to an altered lifespan and cellular metabolism in the nematode, and that the activity of this gene in other animals, such as yeast and in humans, is related to a physiological clock which coordinates aspects of cellular physiology, from cell division, growth, to aging. It is known in the art that mutations in a bacterial homolog *miaA* affect cellular growth in many ways, such as decreased suppression of nonsense mutation, slowed ribosomal translation, etc. The specification also teaches that *miaA* mutations increase the rate of spontaneous mutations. See specification at paragraph bridging pages 18-19, and first full paragraph on page 19. It is also known in the art that mutation in the yeast homolog MOD5 similarly prevented suppression of certain nonsense mutations. As discussed in the previous Amendment,

Golovko et al.[1] ("Golovko") discloses that the human homolog hgro-1 can complement the suppression function of MOD5. Applicants submit that one skilled in the art would believe that a mutation in this highly conserved gene would increase the rate of spontaneous mutation or decrease suppression of nonsense mutation, and that it would reasonably correlate with a mechanism that contributes to the formation of cancer. Hence, there is a substantial and credible utility in monitoring the expression and mutation of hgro-1 in humans.

According to applicable case law, applicants do not have to provide evidence sufficient to establish that an asserted utility is true "beyond a reasonable doubt." *In re Irons*, 340 F.2d 974, 978, 144 USPQ 351, 354 (CCPA 1965). All that is required in evaluating the credibility of an asserted utility is a preponderance of the totality of the evidence under consideration. *In re Oetiker*, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). A preponderance of the evidence exists when it suggests that it is more likely than not that the assertion is question is true. *Herman v. Huddleston*, 459 U.S.375, 390 (1983). Here, Applicants submit that the totality of facts and reasoning suggests that it is more likely than not that the statement of the applicant is true.

The Examiner alleges that disclosure of SEQ ID NO:3 is simply a starting point for further research and investigation into potential practical uses of the claimed nucleic acids. Applicants submit that the Examination Guidelines for the Utility Requirement ("Examination Guidelines") cautioned not to interpret "immediate benefit to the public" to mean that products or services based on the claimed invention must be "currently available" to the public in order to satisfy the utility requirement. *Brenner v. Manson*, 383 U.S., 519, 534-35, 148 USPQ 689, 695 (1966). Rather, any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient, at least with regard to defining a "substantial" utility.

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[1] Golovko et al., "Cloning of a human tRNA isopentenyl transferase", Gene (2000) 258:85-93.

Furthermore, the claimed invention provides more than one utility. According to MPEP 2107.01, an assay method for identifying compounds that themselves have a substantial utility also define a real world context of use. In the present application, the specification discloses that the substrate of IPT is DMAPP which is a precursor of the lipid side-chain of ubiquinone in bacteria, and related to synthesis of cholesterol and its derivatives in eukaryotes (see page 23, first full paragraph). Applicants invite the Examiner's attention to Benko et al.[2] ("Benko"), wherein it is taught that the yeast tRNA biosynthetic pathway and the sterol biosynthetic pathway competes for DMAPP, which is the substrate of MOD5 in yeast. At the time of Benko's publication, the human homolog of MOD5 (i.e., hgro-1) was not known and Benko did not disclose or suggest using hgro-1. Benko discloses an assay that is based on using yeast MOD5 to screen for inhibitors that reduce i^6A modification thereby affecting the distribution of DMAPP between tRNA synthesis and sterol synthesis. Benko indicates that the yeast-based assay can be developed to identify new drugs that can affect the pathways of cholesterol synthesis and synthesis of farnesyl-pyrophosphate-dereived products independently. Applicants submit and one of skill in the art would recognize from the specification that hgro-1 produced by the claimed invention can be used additionally to screen for therapeutic compounds that interfere with cholesterol biosynthesis. Such a utility is well established, specific, has a real world context and is believable to a person of ordinary skill in the art as evidenced by the peer-reviewed publication.

According to the Examination Guidelines for the Utility Requirement ("Examination Guidelines") Examination Guidelines, if the applicant has asserted that the claimed invention is useful for any particular practical purpose and the assertion would be considered credible by a person of ordinary skill in the art, the Examiner should not impose a

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[2] Benko et al., "Competition between a sterol biosynthetic enzyme and tRNA modification in addition to changes in the protein synthesis machinery causes altered nonsense suppression." January 4, 2000, Proc Natl Acad Sci USA. 4;97(1):61-6, submitted herewith as reference BN.

rejection based on lack of utility (66 FR 1098, Jan. 5, 2001). Applicants submit that the claimed invention satisfies the utility requirements under 35 U.S.C. section 101.

In the Office Action, the Examiner contends that it appears from the work of Ushijima et al. that methylation of a specific area of DNA or a specific group of genes is more important than the overall level of DNA methylation in tumors. The Examiner further contends that there are contradictions in the cited published literature and that it can be concluded that DNA methylation and its relationship to cancer is unreliable. Applicants respectfully disagree with these contentions. Even assuming that there are controversies in the literature, the asserted utility is not wholly inconsistent with contemporary knowledge in the art such that the utility is not credible. Applicants point out that these assertions relate to DNA methylation generally and lack specificity with respect to the claimed invention. MPEP 2107.02 (IV) states that it is imperative that Office personnel use specificity in setting forth a rejection under 35 U.S.C. 101. However, these contentions are moot because a patent applicant need show utility for only one disclosed purpose. See *Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 958, 220 U.S.P.Q. 592 (Fed. Cir. 1983), *cert. denied,* 469 U.S. 835 (1984); *Ex parte Lanham*, 121 U.S.P.Q. 223 (Pat. Off. Bd. App. 1958). In view of the evidence and reasoning provided in the foregoing paragraphs, Applicants have showed more than one disclosed utility that meets the utility requirements.

As such, Applicants respectfully request that the rejection under 35 U.S.C. 101 be withdrawn.

5. THE REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, FOR LACK OF ENABLEMENT SHOULD BE WITHDRAWN

Claims 21-24 are also rejected under 35 U.S.C. 112, first paragraph. The Examiner contends that since the claimed invention is not supported by either a credible,

specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Applicants traverse this rejection on the ground that claims 21 to 24 has significant patentable utility as discussed in the Section above. When an Applicant satisfactorily rebuts a rejection based on a lack of utility under 35 U.S.C. § 101, the corresponding rejection imposed under 35 U.S.C. § 112, first paragraph, should also be withdrawn. Thus, Applicants respectfully request that the rejection of claims 21-24 under 35 U.S.C. § 112, first paragraph, be withdrawn.

6. THE REJECTIONS UNDER 35 U.S.C. § 102(b) FOR ANTICIPATION SHOULD BE WITHDRAWN

Claim 22 is rejected under 35 U.S.C. § 102(b) as being anticipated by Hudson ("Hudson", Accession number G24438, May 31, 1996). Applicants respectfully disagree.

Anticipation under 35 U.S.C. § 102 requires identity of invention. The court made it absolutely clear that "anticipation requires that all of the elements and limitations of the claim are found within a single prior art reference ... [and] ... [t]here must be no difference between the claimed invention and the reference disclosure, as viewed by a person or ordinary skill in the field of the invention." *Scripps Clinic & Research Fdn. v. Genentech Inc.*, 927 F.2d 1565, 1576 (Fed. Cir. 1991).

Claim 22 is drawn in part to a complement of a polynucleotide that encodes a polypeptide encoded by SEQ ID NO:3, which polypeptide is the human homolog of the C. elegans GRO-1 protein (hgro-1). The amino acid sequence of hgro-1 is depicted in Figure 9 and is now assigned new SEQ ID NO: 63. In contrast, Hudson discloses human STS WI-12773 which is a complement to only residues 1778-2029 of SEQ ID NO:3. Hudson does not disclose a polynucleotide that encode hgro-1, and thus, does not anticipate claim 22. This rejection is in error, and should be withdrawn.

Claims 23-24 are rejected under 35 U.S.C. § 102(b) as being anticipated by

Bonaldo *et al.* (1996, Genome Research, 1996, vol.6(9), 791-806, "Bonaldo") as evidenced by the sequence database entry accession number BM721352. The Examiner alleges that Bonaldo teaches Homo sapiens cDNA clone UI-E-E01 which comprises residues 1121-1210 of SEQ ID NO:3. The Examiner admits that Bonaldo does not disclose that said clone encodes a fragment comprising a zinc finger motif, and does not disclose that said fragment can rescue the e2400 phenotype, but the disclosed polynucleotide allegedly meets the required limitation of comprising residues 1121-1210 of SEQ ID NO:3, therefore it is reasonable to assume that it would have the same inherent properties of rescuing the e2400 phenotype as claimed. Applicants respectfully disagree.

According to the FEATURES section of sequence entry BM721352, it is stated that UI-E-E01 is a normalized cDNA library (not a cDNA clone as alleged by the Examiner) constructed according to the method taught in Bonaldo. Contrary to the Examiner's allegation, Bonaldo does not disclose human cDNA library UI-E-E01 (see Bonaldo attached hereto as Exhibit A, in particular Table 1 on page 793), and does not disclose any nucleotide sequence of cDNA clone. Thus, Bonaldo does not anticipate claims 23 and 24. The rejection is in error.

Applicants respectfully points out that the sequence entry BM721352 corresponding to clone UI-E-E01-aib-b-20-0-UI was created on March 1, 2002. As such, the public disclosure of the nucleotide sequence in BM721343 postdates February 25, 2000, which is the priority date of the present application. Therefore, sequence entry BM721352 is not prior art to the claimed invention and the rejection is in error.

In view of the foregoing, the rejections under 35 U.S.C. § 102(b) should be withdrawn.

CONCLUSION

Applicants respectfully request that the foregoing amendments and remarks be made of record in the file history of the instant application. Applicants believe that the remarks and amendments made herein now place the pending claims in condition for allowance.

Respectfully submitted,

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Laura A. Coruzzi — 30,742
Laura A. Coruzzi (Reg. No.)

By: T. Christopher Tsang — 40,258
T. Christopher Tsang (Reg. No.)

PENNIE & EDMONDS LLP
1155 Avenue of the Americas
New York, New York 10036-2711
(212) 790-9090